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1639	8

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/763,308	Applicant(s) ARVIDSSON ET AL.	
File Copy	Examiner Jon D Epperson	Art Unit 1639	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *12-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Please note: The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to **Group Art Unit 1639**.

Status of the Application

1. Receipt is acknowledged of a Response to a Restriction Requirement, which was dated on April 25, 20003 (Paper No. 7).

Priority Claims

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in European Patent Office on November 25, 1999. It is noted, however, that applicant has not filed a certified copy of the SWEDEN 9902988-6 (8/24/1999) application as required by 35 U.S.C. 119(b) or PCT Rule 17. Therefore, the effective filing date of the claims is the effective U.S. filing date of the 371 Application i.e., August 21, 2000.

Status of the Claims

3. Claims 1-14 are pending in the present application.

4. Applicant's response to the Restriction and/or Election of Species requirements in Paper No. 7 is acknowledged (Applicants elected Group I, claims 1-11) and claims 12-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected

inventions, there being no allowable generic or linking claim (see below i.e., ***Response to Restriction and/or Election of Species***).

5. Please note: Applicant's elected species (Molecules <1000 Da, 2-hydroxypropyl-β-cyclodextrin) were found in the art, see rejections below. Applicant is reminded of MPEP § 803.02 with respect to species elections:

> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. ***The prior art search, however, will not be extended unnecessarily to cover all nonelected species.*** Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

6. Therefore, claims 1-11 are examined on the merits in this action. Please note that claims 1-11 are only examined to the extent of the elected species and/or subject matter (see MPEP § 803.02).

Response to Restriction and/or Election of Species

7. Applicant's election of Group I (claims 1-11) with traverse in Paper No. 7 is acknowledged.

8. The traversal is on the ground(s) that "Applicants disagree with the assertion made in the Action that EP 0609766 ("Nishiki") discloses cyclodextrin use in a compound library setting.

Nishiki, in fact, discloses cyclodextrin use with a single compound, a myeloperoxidase, not a library of compounds. As such, Applicants disagree with the assertion that the groups lack unity because this technical feature (i.e., a cyclodextrin storage of library members) is disclosed by Nishiki"

9. These arguments were fully considered but were not found persuasive. As stated in Paper No. 5, Nishiki et al does anticipate and/or render obvious the technical feature that links Applicants' claims (see Nishiki et al Art rejection below; please note: that Nishiki et al is but one example disclosing the technical feature that links Applicants' claims, the other 35 U.S.C. § 102 and § 103 Rejections below also show that Applicants' linking technical feature was known in the art) and, as a result, restriction is proper.

10. Applicant's election of species in Paper No. 7 is also acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election of species has also been treated as an election without traverse (MPEP § 818.03(a) and/ or 37 CFR 1.111(b)).

11. As a result, the restriction requirement and/or election of species is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

12. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98 (b) requires a list of all patents, publications, or other information

submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on the form PTO-892, they have not been considered.

Specification

13. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

14. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claims Rejections - 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 1-11 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 USC 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a written description rejection.

These claims encompass a broad genus. For example, claim 1 discloses a library of "compounds" that interacts with cyclodextrin in such a way as to help preserve the library. The scope of this claim includes an infinite number of "compounds." The specification and claims do not place any limit on the number of atoms, the types of atoms, or the manner in which said atoms might be connected to form the "compound" library. Although the specification discloses a few possible "compounds" (see Specification, Examples), the specification and claims do not provide ***any*** guidance as to what structural features ***all*** of these "compounds" share. Consequently, it is not possible to determine *a priori* which compounds would interact with the cyclodextrins (i.e., become encapsulated in the cyclodextrin cavity) and thus be "protected" by the cyclodextrins preservative effects.

The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify ***all*** of the members of the genus or even a substantial portion thereof, and because the genus is enormous and highly variant, Applicants' generic teachings (see specification, Catalysts, pages 6-8) are insufficient to teach the entire genus i.e., ***Applicants' specification does not teach which compounds will be protected by the cyclodextrins***. Consequently, one of skill in the art would reasonably conclude

that the disclosure fails to provide a representative number of species to describe this enormous genus. Thus, applicant was not in possession of the claimed genus.

16. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a few of the compounds that fall within the broad scope of the claimed invention (see below), is not enabling for the vast majority of compounds that fall within this broad scope. This is an enablement rejection.

Any person skilled in the art to which it pertains, or with which it is most nearly connected, would not know how to make and use the claimed invention. Applicant has not provided enough examples of how to use the claimed invention to be enabling for the full breadth of the claims. It is clear from applicants' specification and the teachings of the prior art how one might practice this invention with a library of compounds that can "enter the cyclodextrin cavity", which is the art recognized mechanism by which cyclodextrins protect their respective ligands (e.g., see Tabushi et al, page 1023, Scheme I, compound 18 showing encapsulation of a quinone by a cyclodextrin which afford protection to the quinone from oxidation). However, applicants' has not provided sufficient guidance as to how to make/use **any** of the other compounds that not enter the cyclodextrin cavity and/or bind to the cyclodextrin cavity at all.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the

enablement requirement and whether any necessary experimentation is "undue". These factors include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the level of one of ordinary skill;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) Breadth of the claims and nature of the invention: The breadth of the claims is large because it includes all compounds and hence reads on an infinite number of possibilities.

(3 and 5) The state of the prior art and the level of predictability in the art: The prior art teaches that only compounds that can enter the cyclodextrin cavity will be afforded some level of protection. However, Applicants claims include a large number of compounds (indeed the majority of Applicants' claimed compounds) that would not fall within this class of compounds. Therefore, the level of predictability in the prior art for those compounds is low or absent.

(4) The level of one of ordinary skill: The level of skill required would be high, most likely at the Ph.D. level.

(6-7) The amount of direction provided by the inventor and the existence of working examples: Applicants have not provided any guidance on how to use their invention with a library of compounds that do not enter the cyclodextrin cavity and/or at least bind to the

cyclodextrin. Therefore, the Examiner contends that the vast majority of Applicants' claimed embodiments are inoperative.

(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: The instant specification for all the reasons asserted above does not provide to one skilled in the art a reasonable amount of guidance to use the claimed invention with compounds that do not enter the cyclodextrin cavity. It would take undue experimentation to determine (1) which compounds would enter the cyclodextrin cavity and (2) for those compounds that do not, which would include the vast majority of the compounds that would fall within the scope of Applicants' claims, the invention just doesn't work i.e., if there is no interaction – there can be no protection. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 & n.23 (Fed. Cir. 1991). Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure, one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation.

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 1-11 are rejected under 35 U.S.C. 102(a) as being anticipated by Henco et al (EP 0 947 820 A2) (Date of Publication is **October 6, 1999**).

For ***claims 1-11***, Henco et al (see entire document) discloses the use of cyclodextrins (including Applicant's elected 2-hydroxypropyl-β-cyclodextrin, see claim 7) as additives for compound storage, which anticipates claims 1-11. Please note that the additive is first combined to a solution of the compounds and thus is also prepared (at least for a while) in a wet form. Furthermore, Henco et al discloses 4% by weigh which falls within applicants' claimed specification range (see Henco, claim 8; see also page 4 of Applicants' specification for conversion chart from %wt to mM concentration)

18. Claims 1, 4-9 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Tabushi et al (Tabushi, I.; Yamamura, K.; Fujita, K.; Kawakubo, H. "Specific Inclusion Catalysis by β-Cyclodextrin in the One-Step Preparation of Vitamin K1 or K2 Analogues" *J. Am. Chem. Soc.* **1979**, *101(4)*, 1019-1026).

For ***claims 1, 4-9 and 11***, Tabushi et al (see entire document) discloses adding β-cyclodextrin to a library of Vitamin K analogues to prevent them from H_2O_2 attack (see

Tabushi et al, page 1023, scheme I showing protection of compound(s) **18** from H_2O_2 attack; see also page 1020, column 2, compounds 7 and 8 wherein the R groups are defined; please note that the Vitamin K analogs are less than 1000 Da). Furthermore, Tabushi et al discloses using a 50mM concentration of β-cyclodextrin and also discloses varying the concentration of β-cyclodextrin in relation to the compounds in the library and, as a result, would anticipate any other concentration as well (see Tabushi et al, page 1020, Table 1, superscript "a" denoting the β-cyclodextrin concentration at "5×10^{-2} M"; see also column 2, paragraph 1).

19. Claims 1 and 4-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Castillo et al (WO 98/06381) (Date of Publication is **February 19, 1998**).

For ***claims 1 and 4-11***, Castillo et al (see entire document) discloses the use of cyclodextrins (including Applicant's elected 2-hydroxypropyl-β-cyclodextrin, e.g., see Example 1) with a library of compounds including drug compounds and various preservatives, which anticipates claims 1 and 4-11 (see Detailed Description o Invention). Please note that the additive is first combined to a solution of the compounds and thus is also prepared (at least for a while) in a wet form. Furthermore, Castillo et al discloses between about 0.5% to about 20% (w/w) which falls within applicant's claimed specification range (see Castillo, claim 11; see also page 4 of Applicants' specification for conversion chart from %wt to mM concentration)

20. Claims 1, 4-9 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Nishiki et al (EP 0 609 766 A2) (Date of Publication is **January 27, 1994**).

For ***claims 1, 4-9 and 11***, Nishiki et al (see entire document) discloses the use of cyclodextrins (see Tables 1-3; see also lines 46-53 disclosing Applicants' specified concentrations) to prevent the loss of biological activity and antgenicity of a library of polypeptides that associate together to form a myeloperoxidase (i.e., a myeloperoxidase is comprised of a "library" of polypeptides, specifically 2α and 2β subunits), which anticipates claims 1, 4-9 and 11.

Claim Rejections - 35 USC § 103

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

22. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

23. Claims 1-9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tabushi et al (Tabushi, I.; Yamamura, K.; Fujita, K.; Kawakubo, H. "Specific Inclusion Catalysis by β-Cyclodextrin in the One-Step Preparation of Vitamin K1 or K2 Analogues" *J. Am. Chem. Soc.* **1979**, *101(4)*, 1019-1026) in view of Applicants' admission in the Specification.

For ***claims 1, 4-9 and 11***, Tabushi et al teaches all the limitations stated in the 35 U.S.C. 102(b) rejection above (incorporated in its entirety herein by reference), which anticipates claims 1, 4-9 and 11, consequently, also renders obvious claims 1, 4-9 and 11.

The prior art teaching of Tabushi et al differs from the claimed invention as follows:

For ***claims 2-3***, the prior art teachings of Tabushi et al differs from the claimed invention by not specifically reciting the use of a library comprising at least 1000 members.

However, Specification teaches the following limitations that are deficient in Tabushi et al:

For ***claims 2-3***, the Specification teaches that compound libraries may contain more than 100,000 different compounds and can be used in pharmaceutical applications (see Specification, paragraph 2-3; see especially paragraph 2, lines 10-11, "Compound libraries may for example contain more than 100,000 different compounds").

It would have been obvious to one skilled in the art at the time the invention was made to protect larger libraries (i.e., libraries with more than 100,000 compounds) with the β-cyclodextrins as taught by Tabushi et al because the Specification admits that these libraries can be used for pharmaceutical applications and the Vitamin K analogues disclosed by Tabushi et al represent a pharmaceutical application. Furthermore, one of ordinary skill in the art would have been motivated to use β-cyclodextrins with larger libraries of susceptible quinones to protect more compounds from potential H_2O_2 attack.

24. Claims 1 and 4-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tabushi et al (Tabushi, I.; Yamamura, K.; Fujita, K.; Kawakubo, H. "Specific Inclusion Catalysis by β-Cyclodextrin in the One-Step Preparation of Vitamin K1 or K2 Analogues" *J. Am. Chem. Soc.* **1979**, *101(4)*, 1019-1026) and Castillo et al (U.S. Patent No. 5,985,310) (102(e) Date is ***March 10, 1998***).

For ***claims 1, 4-9 and 11***, Tabushi et al teaches all the limitations stated in the 35 U.S.C. 102(b) rejection above (incorporated in its entirety herein by reference), which anticipates claims 1, 4-9 and 11, consequently, also renders obvious claims 1, 4-9 and 11.

The prior art teaching of Tabushi et al differs from the claimed invention as follows:

For ***claim 10***, the prior art teachings of Tabushi et al differs from the claimed invention by not specifically reciting the use of a 2-hydroxypropyl-β-cyclodextrin. Tabushi et al only recites β-cyclodextrin (see Tabushi et al, page 1020, Table 1,

superscript "a" denoting the β-cyclodextrin concentration at "5×10^{-2} M"; see also column 2, paragraph 1).

However, Castillo et al teaches the following limitations that are deficient in Tabushi et al:

For ***claim 10***, Castillo et al (see entire document) teaches 2-hydroxypropyl-β-cyclodextrin can be used with pharmaceutical formulations (see column 1, lines 27-35).

It would have been obvious to one skilled in the art at the time the invention to use 2-hydroxypropyl-β-cyclodextrin as taught by Castillo in place of β-cyclodextrin et al as taught by Tabushi et al to protect the vitamin K libraries against oxidation because Castillo et al discloses that the 2-hydroxypropyl-β-cyclodextrin is useful in pharmaceutical preparations, which would encompass the vitamin K libraries disclosed by Tabushi et al and because the structures of β-cyclodextrin and 2-hydroxypropyl-β-cyclodextrin are structurally related (i.e., the references represent analogous art). Furthermore, one of ordinary skill in the art would have been motivated to use 2-hydroxypropyl-β-cyclodextrin with the vitamin K libraries because Castillo et al explicitly states that they are good replacements for β-cyclodextrin (see Castillo et al, column 1, lines 27-35, "There have been a number of attempts to derivative cyclodextrins in order to decrease toxicity or increase solubility. For example, hydroxy-propyl-β-cyclodextrin is a derivative which has been shown to have a relatively low toxicity and a high aqueous solubility as compared to the parent compound, β-cyclodextrin") (emphasis added).

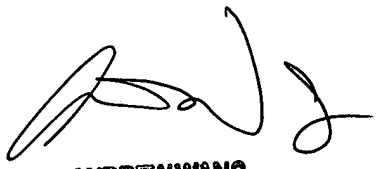
Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (703) 308-2423. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-2439.

Jon D. Epperson, Ph.D.
July 12, 2003



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